REMARKS

The Office action dated July 19, 2011 is acknowledged. Claims 1, 4-6, 8-11, 13-19 and 21-36 are pending in the instant application. Claims 15-19, 30-32 and 36 have been withdrawn from consideration. Claims 1, 4-6, 8-11, 13, 14, 21-29 and 33-35 have been rejected in the present Office action. By the present Office Action response, claim 1 has been amended to recite the active substance as a "pharmaceutical active substance which is present in salt form," support for which may be found throughout the specification such as paragraphs [000016], [000017] and [000023]. As explained in paragraphs [000016] - [000019] of the specification, the pH adjustment is particularly important when the active substance may cause a pH shift due to dissociation of the salt. In addition, the recitation "and wherein said at least one active substance is selected from the group consisting of pharmaceutically active substances and aroma substances" has been deleted. Claim 33 has been canceled.

New claims 37 - 39 have been added. New claims 37 and 38 are based on amended claim 1 except for the following differences:

- Claim 37: The term "multilayered" has been omitted in claim 37. In addition, the pH ranges "between 5.5 and 6.5 (human oral mucosa) and "at about 6" (human nasal mucosa) are omitted.
- Claim 38: The term "multilayered" has been omitted in claim 38.
- Claim 39 is based on paragraph [000050] of the substitute specification.

Reconsideration is respectfully requested in light of the amendments and arguments made herein. No new matter has been added.

Rejection of claims 1, 4-6, 8-11, 13, 14, 21-29 and 33-35 under 35 U.S.C. 103(a)

Claims 1, 4-6, 8-11, 13, 14, 21-29 and 33-35 remain rejected as being unpatentable over U.S. Patent No. 4,572,832 (Kigasawa, et al.) in view of U.S. Publication No. 2003/0099691 (Lydzinski, et al.) and U.S. Patent No. 5,900,247 (Rault, et al.). The Examiner argues that the Kigasawa, et al. reference discloses soft buccal compositions which comprise a medicament to be absorbed through the oral cavity, a water-soluble protein, a polyhydric alcohol and a fatty acid ester and/or a carboxyvinyl polymer. However, the Examiner states that the Kigasawa, et al. reference fails to disclose a matrix-forming polymer according to present claim 1 or a form with one or more aroma substances that does not include a pharmaceutical active substance.

The Examiner refers to Lydzinski, et al. and states that the reference discloses an oral film that is useful for delivering an agent to an animal or human to produce either a therapeutic or cosmetic effect, such as breath fresheners or fragrances, both of which read on the aroma substance of the present claims. The Examiner also states that the active agent can be used in any amount desired, the only limitation being the potential load of the film, but generally that the amounts used will range from about 0.5% to about 15%, with substantially higher amounts for breath fresheners than for pharmaceutical agents.

The Examiner concludes that it would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate an aroma substance in place of the pharmaceutically active ingredient in the compositions of Kigasawa, et al. and to use substances such as pullulan or carrageenan as the base mass material to produce a disintegrating oral film. The Examiner also states that the person with ordinary skill in the art would have been motivated to make those modifications and reasonably would have expected success because the inclusion of an aroma substance (i.e., breath freshener

or fragrance) results in an oral film that quickly disintegrates in the mouth thus leaving the user with fresh or scented breath. The Examiner further argues that carrageenan and pullulan are taught as functionally equivalent to the cellulose and alginic acid materials of Kigasawa, et al. and can also be used in oral film masses while Lydzinski, et al. teach that only an aroma substance need be present in the composition. The Examiner still further argues that the amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize.

The Examiner acknowledges that the combination of teachings of Kigasawa, et al. and Lydzinski, et al. fail to disclose a multi-layer administration form. The Examiner refers to Rault, et al. for teaching a bioadhesive pharmaceutical composition to locally release active ingredients through various mucosal membranes and that the bioadhesive composition comprises a vinyl acetate/polyvinylpyrrolidinone copolymer, at least one active ingredient, optionally a cellulose or cellulose derivative such as ethyl cellulose or hydroxypropylmethyl cellulose and excipients such as plasticizers, flavoring agents or sweeteners. The Examiner concludes that it would have been obvious to one of ordinary skill in the art to prepare a buccal administration form as taught by Kigasawa, et al. and Lydzinski, et al. and to place this material on a protective film as taught by Rault, et al. resulting in a multilayered administration form. The Examiner also states that Rault, et al. provide additional guidance to one of ordinary skill in the art as to the amount of flavoring ingredients, which can include aroma substances, that can be added to such compositions.

Claims 1, 4-6, 9-11, 13, 14, 21-25, 27-29 and 33-35 remain rejected as being unpatentable over U.S. Patent No. 4,764,378 (Keith, et al.) view of Lydzinski, et al. and

Rault, et al. The Examiner states that the Keith, et al. reference discloses buccal dosage forms for transmucosal administration of drugs and thus the pH of the base mass of these dosage forms is approximated or adapted to the physiological values of the mucosa to which the administration form is to be applied. The Examiner acknowledges that the Keith, et al. reference fails to disclose a matrix forming polymer according to present claim 1 or a form with one or more aroma substances that does not include a pharmaceutical active substance.

The Examiner refers to Lydzinski, et al. for disclosing an oral film that is useful for delivering an agent to an animal or human to produce either a therapeutic or cosmetic effect, such as breath fresheners or fragrances, both of which read on the aroma substance of the present claims.

The Examiner concludes that it would have been obvious to the person of ordinary skill in the art to incorporate an aroma substance in place of the pharmaceutically active ingredient in the compositions of the Keith, et al. reference and to use substances such as pullulan or carrageenan in the base mass to produce a disintegrating oral film. The Examiner also argues that there would have been motivation to make those modifications and reasonably would have expected success because the inclusion of an aroma substance results in an oral film that quickly disintegrates in the mouth, leaving the user with fresh or scented breath. The Examiner additionally states that carrageenan and pullulan are taught as functionally equivalent to the cellulose and alginate materials of Keith, et al. and can also be used in oral film masses. The Examiner refers to Lydzinski, et al. for teaching that only an aroma substance need be present in the composition. The Examiner still further argues that the amount of a specific ingredient in

a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize.

The Examiner acknowledges that the combination of teachings of Keith, et al. and Lydzinski, et al. fail to disclose a multi-layer administration form. The Examiner refers to Rault, et al. for teaching a bioadhesive pharmaceutical composition to locally release active ingredients through various mucosal membranes and that the bioadhesive composition comprises a vinyl acetate/polyvinylpyrrolidinone copolymer, at least one active ingredient, optionally a cellulose or cellulose derivative such as ethyl cellulose or hydroxypropylmethyl cellulose and excipients such as plasticizers, flavoring agents or sweeteners. The Examiner concludes that it would have been obvious to one of ordinary skill in the art to prepare a buccal administration form as taught by Keith, et al. and Lydzinski, et al. and to place this material on a protective film as taught by Rault, et al. resulting in a multilayered administration form. The Examiner also states that Rault, et al. provide additional guidance to one of ordinary skill in the art as to the amount of flavoring ingredients, which can include aroma substances, that can be added to such compositions.

Claim 8 remains rejected as being unpatentable over Keith, et al. in view of Lydzinski, et al. and Rault, et al. as applied to claims 1, 4-6, 9-11, 13, 14, 21-25, 27-29 and 33-35 above, and further in view of WO 99/53897 (Bergeron, et al.) and EP 0386960 (Gibson, et al.). In particular, the Examiner states that the Keith, et al. reference discloses buccal dosage forms containing up to 10% by weight active ingredient, in a matrix-forming polymer mass and that the polymer can be alginate, carboxymethyl cellulose, pullulan or carrageenan as taught by Keith, et al. and Lydzinski, et al. The Examiner also

states that an additional protective layer can be provided to the film as taught by Rault, et la. The Examiner acknowledges that Keith, et al. fail to teach the presence of an agent that alters the pH from the Markush group of claim 8.

The Examiner refers to Bergeron, et al. for disclosing a formulation of film-forming ingredient and an active agent for topical formulations and that the pH of the formulation can be adjusted to meet the requirements of the target tissue. For example, formulations applied to the vaginal mucosa a pH of about 4.0-4.5 should be used. The Examiner points out that Bergeron, et al. fail to disclose any agents that would adjust the pH depending on the target tissue.

The Examiner refers to Gibson, et al. for disclosing that the pH of the compositions can be adjusted through the use of pharmaceutically acceptable acids or bases such as sodium or hydrochloric acid and that pH can be maintained by the use of buffering agents.

The Examiner concludes that it would have been obvious to one of ordinary skill in the art at the time of the invention to incorporate a pH adjusting agent in the compositions of Keith, et al. in view of the teachings of Bergeron, et al. and Gibson, et al.

Claim 26 remains rejected as being unpatentable over Keith, et al. in view of Lydzinski, et al., Rault, et al., Bergeron, et al. and Gibson, et al., as applied to claims 1, 4-6, 8-11, 13, 14, 21-25, 27-29 and 33-35 above, and further in view of Kigasawa, et al. In particular, the Examiner states that Keith, et al. disclose buccal dosage forms containing up to 10% by weight active ingredient, in a matrix-forming polymer mass and that the polymer can be alginate, carboxymethyl cellulose, pullulan or carrageenan, as taught by Keith, et al. and Lydzinski, et al. The Examiner also argues that the pH can be adapted

for the target tissue through the use of various ingredients and that an additional protective layer can be provided to the film as taught by Rault, et al.

The Examiner acknowledges that none of the references disclose adjusting the pH using a phosphate buffer.

The Examiner refers to Kigasawa, et al. for disclosing the adjustment of a buccal dosage form containing pindolol using phosphate buffer. The Examiner concludes that it would have been obvious to adjust the pH using phosphate buffer with the motivation being to make such modifications, while the person of ordinary skill in the art would have reasonably expected success since Kigasawa, et al. disclose adjusting the pH of a buccal dosage form using phosphate buffer and Bergeron, et al. disclose that the pH of the dosage form should be adapted to the intended administration site.

It is respectfully submitted that to establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation to modify the reference or to combine the reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. The Applicants respectfully submit that one skilled in the art would have no suggestion or motivation to combine the aforementioned references in order to arrive at the present invention. Additionally, even if one skilled in the art were to consider the teachings of the cited prior art alone or in combination, each and every limitation of the present invention would not be disclosed, nor would there be a reasonable expectation of success if the aforementioned references were to be considered.

The Applicants respectfully disagree with the Examiner's position for at least the

numerous deficiencies of Kigasawa, et al., Lydzinski, et al., Rault, et al. and Keith, et al., that are already of record in the previous Office action responses.

In particular, it is respectfully submitted that, referring to Example 8 of Kigasawa, et al., the Examiner considers that this document discloses an administration form as claimed in present claim 1 since Example 8(b) of Kigasawa, et al. mentions that phosphate buffer (pH 6.5) is used for preparing a mixture containing active substance (pindolol), propylene glycol, fatty acid triglyceride, lecithin and a sucrose fatty acid ester product. However, pindolol is not present in salt form which is in clear contrast to present claim 1 as currently amended. Therefore, Kigasawa, et al. fail to teach pH adjustment in the case where the pharmaceutical active substance is present in salt form. Since pH adjustment is mentioned only in the description of Example 8(b) but nowhere else in the Kigasawa, et al. reference, one skilled in the art would clearly have understood that the use of "phosphate buffer (pH 6.5)" is necessitated by the special mixture of ingredients specified in Example 8(b).

In this connection, it is also submitted that according to Example 8(b) a considerable quantity of gelatin (7.5 g) is added to the mixture containing phosphate buffer (11.75 g; buffer concentration is not specified). Proteins in general, and thus also gelatin, are known to have buffering properties. Therefore, adding the specified quantity of gelatin will be expected to change the pH to which the phosphate buffer was initially adjusted. In conclusion, the base mass which results after adding the matrix polymer (gelatin) in Example 8(b) of Kigasawa, et al., was not approximated or adapted to a specific pH value, and the pH value of this base mass is unknown.

It is further submitted that new claim 37 further limits the pH to "8 to 9" and

"about 4" which further differentiates the claim from the cited prior art.

The Lydzinski, et al. reference fails to make up for the deficiencies of Kigasawa, et al. The Applicants respectfully disagree with the Examiner's statement that "carrageenan and pullulan are taught as functionally equivalent to the cellulose and alginic acid materials of Kigasawa, et al.) (Office action, page 5, last line – page 6, line 2). The Lydzinski, et al. reference teaches films which contain starch as the main component (Abstract; claim 1) and only in such compositions are carrageenan, pullulan, cellulosic materials and alginate taught as functionally equivalent (Lydzinski, et al., page 2, paragraph [0022]) insofar as they may be optionally added in minor amounts to the films which contain starch as the main component. However, Lydzinski, et al. do not teach that these substances are equivalent in general. In addition, since Lydzinski, et al. teach that carrageenan, pullulan, cellulosic materials and alginate may be admixed to the main component (i.e., starch), this would clearly indicate that these substances have properties which are different from starch and thus these substances are not equivalent to starch either.

The Rault, et al. reference fails to make up for the deficiencies of Kigasawa, et al. and Lydzinski, et al. Regarding the limitation "multilayered," the Examiner appears to interpret the "peelable protective film" (col. 2, lines 63-65) of the reference as representing a layer of a multilayered administration form as presently claimed. However, based on the teaching disclosed in the present application, it should be clear that the "multilayer" limitation refers to the fact that the polymer matrix may consist of multiple layers (see, for example, paragraphs [00024], [00050] of the present specification).

In this regard, new dependent claim 39 further recites the multiple layers as individual layers which differ from one another with respect to at least one of the following parameters: active substance content, active substance concentration, content of additives. The "peelable protective film" taught by Rault, et al. does not meet the criteria recited in new claim 39 since it contains neither active substance nor additives.

Regarding the rejection based on Keith, et al., the Examiner states in the Office action (page 7, last three lines) that "Keith, et al. discloses buccal dosage form for transmucosal administration of drugs and thus the pH of the base mass of these dosage forms is approximated or adjusted to the physiological values of the mucosa..." The Applicants strongly disagree with this conclusion since the Keith, et al. reference fails to teach pH measurement or adjustment. The mere fact that the Keith, et al. reference relates to "buccal dosage forms for transmucosal administration" does not support the indirect conclusion that the pH of the base mass of these dosage forms must have been approximated or adjusted to the physiological values of the mucosa. In addition, the Keith, et al. reference fails to teach or disclose any measures or efforts to avoid irritation of the mucosa (i.e., avoiding mucosal irritation) (see, for example, present specification paragraphs [00002], [00012], [00013]) as the reference does not even appear to have been aware of the risk of mucosal irritation.

Regarding the rejections of claims 8 and 26, it is submitted that the claims are dependent from claim 1. As claim 1 is believed to be non-obvious for the reasons stated above, it is submitted that claims 8 and 26 should be considered allowable as dependent from claim 1.

In view of the above, the Applicants respectfully request that the obviousness

rejections be withdrawn.

Conclusion

For the foregoing reasons, it is believed that the present application, as amended, is in condition for allowance, and such action is earnestly solicited. Based on the foregoing arguments, amendments to the claims and deficiencies of the prior art references, the Applicants strongly urge that the obviousness-type rejection and anticipation rejections be withdrawn. The Examiner is invited to call the undersigned if there are any remaining issues to be discussed which could expedite the prosecution of the present application.

Respectfully submitted,

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